Remarks:

Claims 3-4, 8-12, 15-19, 21-25 and 31 remain for consideration in this application with claims 12, 19, and 31 being in independent format. Claims 8-12, 15-19, 21-25 and 31 have been amended; claims 7, 13-14 and 20 have been cancelled. In view of the claim amendments, together with the remarks hereunder, the rejections of the Office Action of August 25, 2006 must respectfully be withdrawn.

Turning now to the Office Action, Applicant notes with appreciation that the Examiner has withdrawn the previous rejections based on the Sheffel reference.

In the Office Action, claim 12 was objected to because the word assay was misspelled. Applicant has amended Claim 12 to correct this misspelling, thus, the objection must be withdrawn.

In the Office Action, claims 3-4, 7-25 and 31 were rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,683,864 to Houghton et al. (hereinafter Houghton), and further in view of Teo et al. (hereinafter Teo) and Lazizi et al. (hereinafter Lazizi). Houghton discloses combinations of HCV antigens for use in immunoassays for detecting HCV antibodies in a serum sample. The Examiner conceded that Houghton does not teach or suggest "determining the optical density of the sample" or provide "an OD value that correlates to chronic HCV." Office Action page 3, ¶ 3. Yet, the Examiner contended that this correlation and the use of OD values to predict chronic HCV would have been obvious in view of the Teo and Lazizi references, which each disclose the use of multi-antigen arrays to screen for HCV antibodies utilizing OD measurements. Office Action page 4, P 1. According to the Examiner, Teo teaches that "'high OD readings' are equated to HCV antibody positive," and Lazizi teaches that "[i]n chronically HCV-infected patients, high levels of

anti-HCV antibodies are often associated with the presence of HCV RNA sequences in sera." Office Action page 4, P1. From these teachings, the Examiner concluded that it would have been obvious to combine the methods of Houghton, Teo and Lazizi "in order to quantify antibody-antigen complexes in an assay to determine whether an individual is chronically infected by HCV." Office Action page 4, P. 2. Moreover, the Examiner alleged that one would be motivated to do so based on the objective stated in the Teo reference, which was to "devise a scheme in which results validated by enzyme immunoassay (EIA) would not require costly and methodically elaborate supplemental assays." Further, the Examiner asserted that there would have been an expectation of success because the techniques involved are all well-known. Applicant contends that the Examiner is using impermissible hindsight reconstruction to selectively pick portions of each reference favorable to the rejection, while ignoring conflicting teachings therein. Prior art references must, however, be considered in their entirety, including portions that would lead away from the claimed invention. W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). Applicant submits that when taken as a whole, no combination of Houghton, Teo or Lazizi can be said to render the present invention obvious.

To establish a *prima facie* case of obviousness, the prior art references, either alone or in combination, must teach or suggest all of the claim limitations. There also must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine reference teachings to arrive at the claimed invention. And there must be a reasonable expectation of success. M.P.E.P. § 2143. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both

be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). For at least the reasons detailed below, Applicant asserts that the Examiner has failed to establish a *prima facie* case of obviousness based on the combination of Houghton, Teo and Lazizi.

First, there is no suggestion or motivation to combine the teachings of Houghton, Teo and Lazizi to arrive at the claimed invention. The Examiner alleged that one would have been motivated to combine the reference teachings to determine whether an individual is chronically infected by HCV because Teo suggests the need for less complicated, inexpensive EIA validation methods and that there would have been an expectation of success because the techniques involved are all well-known. Office Action page 4, P. 2. Without conceding the point, Applicant submits that even if it would be obvious to try to develop a less costly and more efficient test of any kind, that does not automatically render every inexpensive/more efficient test obvious. "'Obvious to try' has long been held not to constitute obviousness." In re O'Farrell, 853 F.2d 894, 903, 7 U.S.P.Q.2d 1673, 1680-81 (Fed. Cir. 1988). "A general incentive does not make obvious a particular result, *nor does the existence of techniques by which those efforts can be carried out.*" In re Deuel, 51 F.3d 1552, 1559 (Fed. Cir. 1995). Moreover, Applicant contends that the suggestion in Teo of devising a method to efficiently validate EIA results would not provide the requisite motivation, as suggested by the Examiner, because the problems associated with determining and/or confirming HCV-positive or -negative results are separate and distinct from the problem of determining whether a *known* HCV-positive sample is chronically infected. Accordingly, Teo cannot provide the requisite motivation

to combine the teachings of these references to arrive at the claimed invention, and the rejection must be withdrawn.

Second, even if there was such a motivation, the prior art references relied on by the Examiner fail to teach or suggest, either alone or in combination, each and every limitation of the claims of the present application. For example, independent claim 12 recites the limitation of "optical density ranges corresponding to certain probabilities that the individual has chronic HCV infection" which have "at least 80% accuracy levels for any measured optical density level." Independent claim 19 recites the limitation of "a set of standard optical density values correlated with probabilities of chronic HCV infection" which can be used to predict whether an individual has chronic HCV infection. Finally, independent claim 31 recites the limitation of predicting chronic HCV infection by comparing the optical density of a sample to a "correlation curve based on the optical densities of fluid samples in combination with HCV antigen from an HCV antibody-based assay from individuals having chronic HCV infection and individuals that have cleared the HCV infection but still test positive for HCV antibodies." In the Office Action, the Examiner conceded that Houghton does not disclose the use of optical density for measuring assay reactivity and does not provide an OD value that correlates with chronic HCV infection, and therefore, cannot be said to teach or suggest the limitations of the claims. However, the Examiner alleged that this deficiency was met by the teachings of Teo and Lazizi.

Applicant maintains that neither the Teo reference nor the Lazizi reference can cure the deficiencies of the Houghton patent with respect to the present invention. Although the Teo reference notes that moderate to strong OD readings can be considered positive for HCV antibodies,

the reference provides no teaching or suggestion of optical density ranges, values or of a correlation curve which correspond to probabilities of chronic HCV infection for predicting whether an individual has chronic HCV infection, as recited in independent claims 12, 19 and 31. Likewise, although indicating that in *chronically HCV-infected individuals,* high levels of anti-HCV antibodies are often associated with the presence of HCV RNA sequences," Lazizi does not teach or suggest optical density ranges, values or a correlation curve which correspond to probabilities of chronic HCV infection for predicting whether an individual has chronic HCV infection, as recited in independent claims 12, 19 and 31. Moreover, the observation in Lazizi is limited individuals already known to be chronically infected, and there is no teaching or suggestion in Lazizi that would enable a person of ordinary skill in the art to determine that the individual is chronically infected to begin with, other than by conventional PCR techniques disclosed therein. Because Houghton, Teo and Lazizi fail to teach or suggest each and every limitation of the present claims, these references cannot sustain a *prima facie* case of obviousness.

Furthermore, there is nothing in Houghton, Teo or Lazizi that would enable a person of ordinary skill in the art to predict whether an individual has chronic HCV infection, because these references provide no teachings beyond determining whether a sample is in fact, HCV-positive. As explained in the present application, merely knowing that a sample is positive for HCV antibodies does not allow one to differentiate between individuals that were infected but recovered from the infection, and individuals that are chronically infected. Neither Houghton, nor Teo nor Lazizi are concerned with discerning and predicting chronic HCV infection, as recited in the claims. Rather, they are concerned only with detecting and confirming the presence of HCV antibodies in a sample,

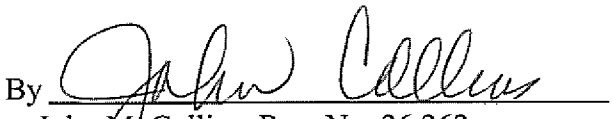
and each reference approaches the problem differently. Houghton discloses the use of a multi-antigen array that provides more efficient detection of HCV antibodies when compared to single antigen arrays. Teo approaches the problem by attempting to confirm the accuracy of two second generation anti-HCV EIAs by cross-validation and supplemental testing using samples from high risk individuals; ultimately concluding that the two EIAs are divergent in terms of specificity and sensitivity, resulting in a high incidence of false positives. See page 219. Lazizi is concerned with comparing the specificity of first generation anti-HCV ELISA to a second generation anti-HCV EIA, and a second generation RIBA II. However, both Teo and Lazizi ultimately suggest that PCR is the more accurate validation method and indeed, that is the prevalent validation technique utilized today. Specifically, the Teo reference indicates that instead of the cross-validation scheme devised in Teo, amplification of HCV RNA with PCR could be used to validate EIA reactivities (although PCR technology at the time was limited to the patent holders) (see page 918), and Lazizi uses nested PCR as the reference test to clarify discrepancies between the ELISA, EIA and RIBA II test results, ultimately concluding that "PCR remains the reference assay." See Abstract. Inherent in each reference is the teaching that immunoassays are unreliable indicators of HCV infection, and given this unreliability, a person of ordinary skill in the art would not be motivated by these teachings to utilize these immunoassays for more specific analysis beyond HCV-positive or -negative. There certainly would have been no motivation and no reasonable expectation of success that these immunoassays could be used to predict and determine chronic HCV infection. When taken as a whole Houghton, Teo and Lazizi, either or alone or in combination, fail to teach or suggest each and

every limitation of the present claims. Accordingly, it cannot be said that the claims are obvious in view of these references and such rejection must be withdrawn.

In view of the foregoing, a Notice of Allowance appears to be in order and such is courteously solicited. If any questions should remain, the Examiner is encouraged to contact the undersigned at 1-800-445-3460.

Any additional fee which is due in connection with this amendment should be applied against our Deposit Account No. 19-0522.

Respectfully submitted,

By 

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